Claims

1. A therapeutic composition effective on contact with thrombin at a site of treatment in a patient as a tissue adhesive, hemostat or sealant, said composition comprising non-autologous, non-single donor mammalian fibrinogen that is capable of polymerizing when provided in solution at said site at a concentration of about 10 mg/ml thereof or less, to a fibrin network having therapeutically effective strength, and further comprising a sufficient amount of one or more physiologically-compatible solutes such that said composition, if formulated as a lyophilized material, can be reconstituted therefrom at room temperature in sterile water for injection in about 30 minutes or less, at about 25 mg/ml of said fibrinogen.

2. A therapeutic composition effective on contact with thrombin at a site of treatment in a patient as a tissue adhesive, hemostat or sealant, said composition comprising non-autologous, non-single donor mammalian fibrinogen that is capable of polymerizing when provided in solution at said site at a concentration of about 30 mg/ml thereof or less, to a fibrin network having therapeutically effective strength, wherein said composition contains less than about 30% (w/w), based on total protein mass present therein, of proteins other than fibrinogen, and further comprises a sufficient amount of one or more low molecular weight

physiologically-compatible solutes such that said composition, if formulated as a lyophilized material, can be reconstituted therefrom at room temperature in sterile water for injection in about 30 minutes or less, at about 25 mg/ml of said fibrinogen.

3. A therapeutic composition according to Claim 2 prepared as a lyophilized material.

4. A therapeutic composition according to Claim 3 wherein said sufficient amount of solute comprises between about 0.10 mg and about 0.50 mg of sodium citrate per mg of fibrinogen.

5. A therapeutic composition according to Claim 3 wherein said sufficient amount of solute comprises between about 0.075 mg and about 1.0 mg of epsilon-aminocaproic acid per mg of fibrinogen.

6. A therapeutic composition according to Claim 4 wherein said sufficient solute further comprises, per mg of fibrinogen, between about 0.075 mg and about 1.0 mg of epsilon-aminocaproic acid.

7. A therapeutic composition according to Claim 2 capable of said polymerization when said fibrinogen thereof is made present at said site of treatment at a concentration of about 10 mg/ml or less.

8. A therapeutic composition according to Claim 2 prepared as a solution.

9. A therapeutic composition according to Claim 8 that is frozen.

10. A therapeutic composition according to Claim 2 containing bovine fibrinogen.

11. A therapeutic composition according to Claim 2 capable of undergoing said effective polymerization at said treatment site when made present at a concentration thereof that provides between about 5 mg/ml and about 30 mg/ml of clottable fibrinogen.

12. A fibrinogen-containing therapeutic composition according to Claim 2 comprising, as percent by weight of total protein contained therein,

clottable fibrinogen, at about 56% or greater;
serum albumin, at less than about 20%;
gamma globulin, at less than about 10%;
plasminogen, at less than about 1%; and
plasma fibronectin, at less than about 3%.

13. A reactive therapeutic composition effective on contact at a site of treatment in a patient as a tissue adhesive, hemostat or sealant, said composition comprising, per milliliter thereof, between about 0.05

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and about 500 NIH units of thrombin and also, per milliliter, between about 5 and about 30 mg of fibrinogen capable of being polymerized to a fibrin network having therapeutically effective strength, when present at said site at said concentration.

14. A method for maintaining the therapeutic effectiveness of a composition according to Claim 8 comprising the step of maintaining said solution at a pH of between about 7.5 and about 8.5.

15. A method for producing a therapeutic fibrinogen composition comprising three or more steps including at least the steps of:

(A) precipitating fibrinogen from a sample of mammalian blood plasma with polyethylene glycol 1000;

(B) resuspending said fibrinogen in solution; and

(C) reprecipitating said fibrinogen with glycine;

wherein precipitation of said fibrinogen with polyethylene glycol is performed only once.

16. A method according to Claim 15 wherein at least about 90% of the fibrinogen present in said sample is recovered.

17. A therapeutic composition produced according to the method of Claim 15.

18. A method for inducing tissue adhesion, sealing of tissue, or hemostasis in a mammalian patient at a site of treatment therein comprising contacting said site with a therapeutically effective amount of a therapeutic composition according to Claim 2.

19. A method according to Claim 18 further comprising contacting said site or said composition with an amount of thrombin effective to convert fibrinogen of said composition to a fibrin network having therapeutically effective strength.

20. A method according to Claim 19 wherein the amount of thrombin utilized therein is from about 0.1 NIH unit up to about 1000 NIH units thereof per milliliter of fibrinogen-containing therapeutic composition utilized therein.

21. A method according to Claim 20 wherein said amount of thrombin is from about 1.0 NIH unit up to about 300 NIH units thereof.

22. A method according to Claim 19 wherein said thrombin and said fibrinogen-containing therapeutic composition are applied separately to said site of treatment.

23. A method according to Claim 19 wherein said thrombin and said fibrinogen-containing therapeutic composition are applied concurrently to said site of treatment.

24. A method according to Claim 19 wherein said thrombin and said fibrinogen-containing therapeutic composition are first combined and then applied to said site of treatment.

25. A method according to Claim 18 wherein said fibrinogen-containing therapeutic composition that contacts said site of treatment is in the form of a dry lyophilized powder.

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